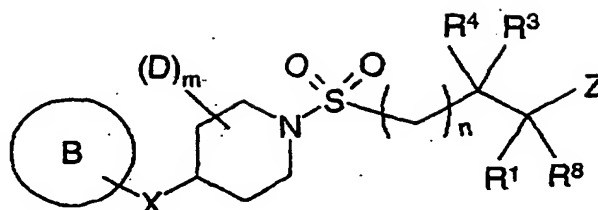


CLAIMS:

What we claim is:-

1. A compound of formula (1):



formula (1)

wherein:

Z is selected from $-\text{CONR}^{15}\text{OH}$ and $-\text{N}(\text{OH})\text{CHO}$;

R^{15} is hydrogen or C_{1-3} alkyl;

R^1 is hydrogen or a group selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{5-7} cycloalkenyl, aryl and heteroaryl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl (optionally substituted by one or more R^{17}), aryl (optionally substituted by one or more R^{17}), heteroaryl (optionally substituted by one or more R^{17}), heterocyclyl, C_{1-4} alkoxycarbonyl, $-\text{OR}^5$, $-\text{SR}^2$, $-\text{SOR}^2$, $-\text{SO}_2\text{R}^2$, $-\text{COR}^2$, $-\text{CO}_2\text{R}^5$, $-\text{CONR}^5\text{R}^6$, $-\text{NR}^{16}\text{COR}^5$, $-\text{SO}_2\text{NR}^5\text{R}^6$ and $-\text{NR}^{16}\text{SO}_2\text{R}^2$;

R^{16} is hydrogen or C_{1-3} alkyl;

R^{17} is selected from halo, C_{1-6} alkyl, C_{3-6} cycloalkyl and C_{1-6} alkoxy;

R^2 is group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl where the group is optionally substituted by one or more halo;

R^5 is hydrogen or a group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl where the group is optionally substituted by one or more halo;

R^6 is hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl;

or R^5 and R^6 together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

R^8 is hydrogen or a group selected from C_{1-6} alkyl, C_{3-7} cycloalkyl and C_{5-7} cycloalkenyl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy and C_{1-4} alkyl;

-71-

~~R³ and R⁴ are both hydrogen;~~

n is 0 or 1;

m is 0 or 1;

D is hydrogen, C₁₋₄alkyl, C₃₋₆cycloalkyl or fluoro;

5 X is O, S, SO or SO₂;

B is monocyclic aryl or heteroaryl where each is substituted in an ortho position by, and is optionally further substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C₁₋₄alkyl (optionally substituted by R¹³), C₂₋₄alkenyl (optionally substituted by R¹³), C₂₋₄alkynyl (optionally substituted by R¹³), C₃₋₆cycloalkyl (optionally substituted by R¹³), C₃₋₆cycloalkenyl (optionally substituted by R¹³), phenyl (optionally substituted by halo or C₁₋₄alkyl), heteroaryl (optionally substituted by halo or C₁₋₄alkyl), heterocyclyl (optionally substituted by halo or C₁₋₄alkyl), C₁₋₄alkylthio, C₃₋₆cycloalkylthio, -SOR¹³, -SO₂R¹³, -SO₂NHR¹³, -SO₂NR¹³R¹⁴, -NHSO₂R¹³, -NR¹³SO₂R¹⁴, -NHCONHR¹³, -NHCONHR¹³R¹⁴, -OR¹³, cyano, -CONR¹³R¹⁴, -NHCOR¹³, -CO²R¹³ and -

15 CH₂CO₂R¹³;

or B is bicyclic aryl or heteroaryl where each is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C₁₋₄alkyl (optionally substituted by R¹³), C₂₋₄alkenyl (optionally substituted by R¹³), C₂₋₄alkynyl (optionally substituted by R¹³), C₃₋₆cycloalkyl (optionally substituted by R¹³), C₃₋₆cycloalkenyl (optionally substituted by R¹³), C₁₋₄alkylthio, C₃₋₆cycloalkylthio, -SOR¹³, -SO₂R¹³, -SO₂NHR¹³, -SO₂NR¹³R¹⁴, -NHSO₂R¹³, -NR¹³SO₂R¹⁴, -NHCONHR¹³, -NHCONHR¹³R¹⁴, -OR¹³, cyano, -CONR¹³R¹⁴ and -NHCOR¹³;

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R¹³ and R¹⁴ are independently hydrogen, C₁₋₆alkyl or C₃₋₆cycloalkyl;

or R¹³ and R¹⁴ together with the nitrogen to which they are attached form a heterocyclic 4 to

25 7-membered ring.

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein B is phenyl or pyridyl where each is substituted in an ortho position by, and is optionally further substituted by one or more groups independently selected from halo, trifluoromethyl, cyano, C₁₋₄alkoxy, C₁₋₄alkyl, nitro, aryl, heteroaryl, heterocyclyl, *N*-(C₁₋₄alkyl)carbamoyl and *N,N*-(C₁₋₄alkyl)₂carbamoyl; or B is naphthyl, quinolinyl, thieno[2,3-*d*]pyrimidinyl or thieno[3,2-*d*]pyrimidinyl each being

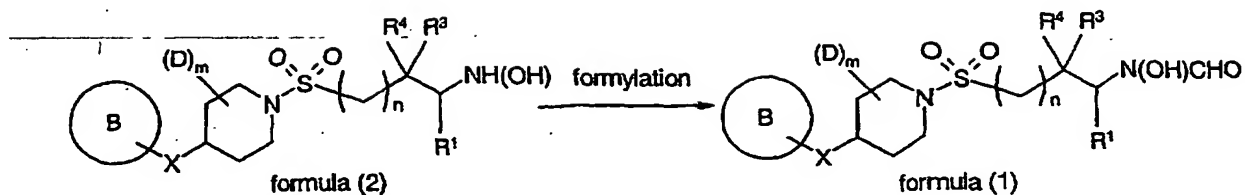
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-72-

optionally substituted by one or more groups independently selected from halo, trifluoromethyl, cyano, C₁₋₄alkoxy, C₁₋₄alkyl, aryl, heteroaryl, heterocyclyl and nitro.

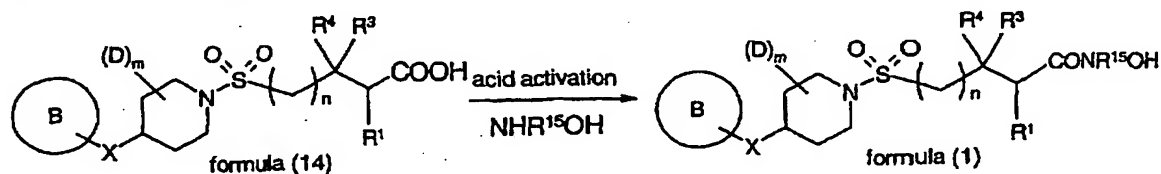
3. A compound according to claim 1 or 2 wherein R¹ is a group selected from C₁₋₆alkyl,
5 C₃₋₆cycloalkyl, aryl, heteroaryl and C₁₋₆alkyl substituted by aryl or heteroaryl wherein any R¹
group is optionally substituted by one or more substituents independently selected from halo,
C₁₋₄alkoxy, C₁₋₄alkyl and C₃₋₆cycloalkyl.
4. A compound according to any one of claims 1 to 3 wherein X is O.
- 10 5. A compound according to any one of claims 1 to 4 for use as a medicament.
6. The use of a compound according to any one of claims 1 to 4 in the manufacture of a
medicament in the treatment of a disease condition mediated by one or more
15 metalloproteinase enzymes.
7. The use of a compound according to any one of claims 1 to 4 in the manufacture of a
medicament in the treatment of a disease condition mediated TNF α .
- 20 8. A pharmaceutical composition comprising a compound according to any one of claims
1 to 4; and a pharmaceutically-acceptable diluent or carrier.
9. A method of treating autoimmune disease, allergic/atopic diseases, transplant
rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy
25 in a warm-blooded animal, such as man, in need of such treatment which comprises
administering to said animal an effective amount of a compound according to claim 1.
10. A process for preparing a compound of formula (1) according to claim 1 comprising,
when Z is -N(OH)CHO, the step of:
30 a) converting a hydroxylamine of formula (2) into a compound of formula (1);

-73-



or when Z is -CONR¹⁵OH, the step of:

b) converting an acid of formula (14) into a compound of formula (1);



5 and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.